Schizophrenia: Current Concepts and Approaches to Patient Care

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Schizophrenia is the most serious of all mental conditions. It is typically a long-lasting condition characterized by repeated relapses and by marked functional impairment. Genetic and environmental factors are important. Exactly which factors and how these combine to cause schizophrenia is still unclear. Antipsychotic medications form the bedrock for treatment. These drugs are effective, but not entirely so, and are associated with negative side effects. Individual differences among the available medications suggest that trials with a different medication may be appropriate when one agent fails or is not appropriate for the specific patient. Monitoring for side effects is important to ensure efficacy and compliance. Often, patients choose to stop taking their medications for a variety of reasons, which invariably will lead most patients to a relapse of illness. Beyond medications, patients need considerable support and specialized services. Families are a key resource. The recent focus on personal determination has led to recovery-based services, including the incorporation of peer support into patient care. [*AHDB*. 2008;1(4):13-22.]

Schizophrenia is a poorly understood condition. Despite several recent documentaries and movies depicting the course and disability of this illness, the lay public remains largely confused about schizophrenia and continues to harbor notions that it is a "split personality" or a "Jekyll and Hyde" phenomenon. Regrettably, efforts to articulate a clear account of what schizophrenia really is and what causes it have been hampered by a lack of compelling evidence as to its etiology. Despite the many clues to the cause(s) of schizophrenia, definitive evidence is still lacking. In many ways, we can be more dogmatic about what is not relevant to schizophrenia (**Table 1**). This is important because stigma, which is fueled by a lack of knowledge, is a major obstacle in managing schizophrenia. Several books provide comprehensive information about schizophrenia.[1-4] This article offers a current overview of schizophrenia and its treatment.

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Diagnosis

Schizophrenia is a complicated diagnosis. The condition is characterized by delusions (fixed, false beliefs), hallucinations (typically "hearing voices" when no one is around), disturbances of speech (illogicality, nonlinearity of thought and conversation), restricted affect and emotionality, and impairments of thinking (memory, attention, reasoning, awareness).

Table 1 Dispelling Common Myths about Schizophrenia

1. Despite common belief, schizophrenia is NOT caused by:
   - "Difficult" parents
   - Diet
   - Stress
   - The left side of the brain dominating the right side
2. It is not a split personality
3. Not all patients are violent
4. Patients are not "inventing" unusual ideas or lying, they believe these

KEY POINTS

- Schizophrenia is the most serious of all mental conditions and is characterized by repeated relapses and significant functional impairment.
- Diagnosis requires a psychotic episode that lasts at least 6 months.
- Continuous use of antipsychotic medications is the mainstay of therapy.
- Patient lack of compliance will inevitably lead to relapse and may have serious consequences.
- The new-generation antipsychotics are slightly more effective but their metabolic side-effect profile is a serious concern, requiring ongoing monitoring by the treating physician.

Table 2 Diagnostic Features of Schizophrenia

1. Characteristics:
   - Cognitive impairment: poor attention, memory, abstract thinking
   - Delusions: bizarre; bodily; grandiose; jealousy; persecutory; religious
   - Hallucinations: auditory; gustatory; tactile; visual
   - Thought disorders: illogicality
   - Blunted affect and restricted emotionality, motivation, and enjoyment
   - Decline in social and/or occupational functioning
2. Features are NOT caused by:
   - Medical conditions
   - Mood disorder
   - Substance abuse
3. Features are present continuously for at least 6 months

Given the impact of such a constellation of symptoms, the condition is typically associated with a decline in social and/or occupational performance. Indeed, this may be what parents, friends, or coworkers notice first—a withdrawal, dropping out of college, or inability to cope with the stress of work. For many patients, the onset of such "disintegration" is insidious. Others have a florid presentation, manifest by prominent delusions, hallucinations, and bizarre behaviors, such as locking oneself in an elevator at a mall and shouting out, "Aliens, go away."

Although such a presentation may lead some to wonder "how hard can it be to diagnose this person as psychotic," the presentation could (and in fact is likely to be complicated by abuse of drugs. This complicates things considerably. Also, many people who develop schizophrenia become depressed as the illness evolves. It can be difficult to determine whether the person is suffering from major depression or is in the early stages of a psychotic illness. It is therefore best to wait and see how things play out definitively over months before making such a serious diagnosis as schizophrenia (**Table 2**).

Table 3 Risk of Developing Schizophrenia If Blood Relative Is Ill

Relationship to relative	Rate, %
Monozygotic (identical) twin	48
Child of parent	14
Sibling	10
Parent	5

Source: Gottesman II, Shields J. Schizophrenia: *The Epigenetic Puzzle*. Cambridge University Press, Cambridge, UK; 1982.

Schizophrenia typically begins in adolescence or in early adulthood. It occurs equally in males and females, but the onset is on average 4 years later in females, and the illness tends to be milder in females. The reasons for these gender differences are not yet known.

Practically, the *Diagnostic and Statistical Manual of Mental Disorders* mandates that clinicians classify this illness as "schizophreniform disorder" if the duration is less than 6 months.[5] This is because some patients have a single psychotic episode, which looks indistinguishable from schizophrenia, but they will regain normal functioning without any recurrence. Similarly, those who abuse drugs such as cannabis can have a psychotic break that appears like schizophrenia, but they, too, will regain normal functioning without further episodes once they quit taking the drugs. This latter condition is classified as a "drug-induced psychosis."[6]

Causes(s) of Schizophrenia

Ultimately, we do not know what causes schizophrenia,[1,7,8] but we do know that it runs in families and is associated with birth complications, head injury, epilepsy, and drug abuse. Cannabis abuse raises one's risk for schizophrenia by about 4.5-fold. Recent research suggests that people who have a genetic vulnerability are 16 times more likely to become psychotic when they abuse cannabis.

An ongoing debate about the causes of schizophrenia is whether any particular insult (eg, genetic defects, birth complications) leads to this condition (like the model of multiple causes of elevated blood pressure) or,

alternatively, whether each of these insults can cause a psychotic condition that has a different cause but is similar in presentation and fits under the rubric of schizophrenia (as in pneumonia, whether caused by influenza virus or by bacteria).

Genetic component

Whether schizophrenia is a single illness or multiple illnesses has not yet been teased out, but we do know it has a strong genetic basis, which puts blood relatives at risk (**Table 3**). Genetic studies have shown abnormalities on several chromosomes (eg, chromosome 5, 8, 11, 13, 22).[9] However, as with many aspects of schizophrenia, the findings are inconclusive and do not point to a precise gene involved. More recent genetic studies have focused on the search for abnormalities in genes or their related proteins that are involved in neuronal development (eg, dysbindin, neuregulin, *SNAP-25*, brain-derived neurotrophic factor).[10]

Birth factors

One of the most reproducible findings in schizophrenia is that affected patients are far more likely to have been born in the first 3 months of the year—the so-called season of birth effect.[11] This curious, yet robust, association points to birth or to the time in utero as relevant to the development of schizophrenia.

Another reproducible finding is that about 20% of people who develop schizophrenia have had some sort of birth complication,[12] such as a prenatal exposure to influenza, haemolytic anemia, severe malnutrition, preeclampsia, asphyxia, or fetal distress. This could, of course, have something to do with the pregnancy and with the delivery itself. For example, the fetus may experience hypoxia in the birth canal, which could result in minimal brain damage that manifests later in adolescence as schizophrenia. Alternatively, the birth complication may occur because the fetus itself is "defective." Brain development in utero might have gone wrong in some way because of genetic misprogramming or because of some external injury (eg, a mother with an infection during the critical first 3 months of pregnancy).

Brain abnormalities

There is evidence that brain development is disturbed in schizophrenia. The evidence comes from postmortem brain studies of people with schizophrenia who died from natural causes (eg, a heart attack, although this could also influence or bias postmortem brain findings) or from suicide (clearly, this could affect the brain).[10,13] Although this type of research has its own methodological problems, these studies have shown convincing evidence of abnormal (underdeveloped) cells and of cells that are misplaced or misaligned in the brains of people with schizophrenia.[10,13]

Table 4 Abnormal Brain Structure Findings in Imaging Studies of Patients with Schizophrenia

Brain area	Percent change*: increased (↑) or decreased (↓), %
Whole brain gray matter	↓5
Whole brain white matter	↓5
Thalamus	↓5
Globus pallidus	↑20
Frontal lobe	↓8
Temporal lobe	↓6
Hippocampus	↓9
Lateral ventricles	↑15
Third ventricle	↑15
Fourth ventricle	↑8

*These findings are (1) estimates from overall research literature; (2) not seen in all patients; (3) not seen all together; (4) not "diagnostic" of schizophrenia; (5) most often not noticeable on a clinical scan but are the result of research involving imaging scans from hundreds of patients.

Sources: References 13, 14.

These subtle findings occur more often in the temporal lobes than in any other brain regions. Modern brain imaging techniques (eg, magnetic resonance imaging [MRI]) facilitate the study of live brains of people with schizophrenia, revealing fairly reproducible findings (**Table 4**).[14,15] Some studies have also included relatives of patients with schizophrenia as a comparison group.[16,17] These reveal much milder, but the same, findings in healthy relatives (who "do not have the illness" but may have genes susceptible to schizophrenia). This raises the question whether such brain abnormalities are present from birth or even before the onset of schizophrenia.

There have been efforts to tease this out. Studies of patients in their first episode of psychosis show the same patterns of abnormalities on brain imaging,[18] but in a more attenuated form, as seen in first-episode patients with chronic schizophrenia. Other studies involve "prodromal" populations, namely, patients who have not had a psychotic episode yet but who show "mild" signs of schizophrenia (eg, oddities of thought and speech). These patients show even "milder," barely detectable, brain abnormalities. In one such study,

Table 5 Evidence for Schizophrenia as a Neurodevelopmental Disorder

1. Genes that code for neurodevelopment have been implicated
2. High rates of birth complications
3. Season of birth phenomenon
4. Many patients have minor physical anomalies*
   - Abnormal or fused webs at toes
   - Abnormal palmar creases
   - Low-set ears
   - Shortened faces
   - Widened eyes
5. Many patients have abnormal fingerprints*
6. Type and pattern of structural brain abnormalities seen in brain-imaging studies
7. Type and pattern of brain changes in postmortem studies

*Subtle skin "blemishes" that relate in timing to maturation of the skin and the central nervous system in utero.

Table 6 Elements of Comprehensive Care for Patients with Schizophrenia

Access to coordinated substance abuse services
Appropriate medication treatment
Counseling: supportive psychotherapy
Good medical care
More specialized counseling/support:
Cognitive behavioral therapy
Peer support services
Psychoeducation (illness education)
Social skills training and community reintegration support services
Financial aid
Housing support
Sheltered and "regular" employment opportunities
Support and educational opportunities

the prodromal patients who went on to have a psychotic break had more temporal lobe abnormalities on MRI than patients who did not progress to psychosis.[19]

Collectively, these findings, which point to faulty early brain development, have led many to consider that schizophrenia may be a neurodevelopmental disorder (**Table 5**).[1,7,20] That is, people with schizophrenia may have an aberrant development of brain "hardwire" (eg, misplaced, misaligned, or immature cells; faulty neural communication tracks). It is postulated that as time goes by, these cortical vulnerabilities become exposed as the patient progresses toward psychosis. Some have suggested that the reason for the onset of psychosis at adolescence is a clue. This is a time of brain "rewiring" and plasticity. With these changes, the otherwise "dormant" brain abnormalities are now exposed. Others have postulated that given this brain vulnerability from birth, other events (eg, drug abuse, stress) during adolescence may also push the person (ie, brain) "over the edge" to cause psychosis. This "2-hit" notion is also an intuitively appealing hypothesis. All these reflect the notion that schizophrenia is a neurodevelopmental disorder, and as with other such disorders (eg, cerebral palsy), the causes may be genetic, environmental, or both.

Kraepelin, the German psychiatrist who first described schizophrenia in 1896, considers this to be a dementing condition. He describes how schizophrenia evolves in adolescence and progresses inexorably into a chronic state (which he called "dementia praecox," dementia of youth).

Seemingly in direct opposition to the brain-imaging evidence that supports the neurodevelopmental hypothesis in schizophrenia, other, long-term imaging studies report a progressive loss of brain tissue.[21,22] This would favor a neurodegenerative hypothesis of schizophrenia (like Huntington's disease). Some have suggested that schizophrenia may have both neurodevelopmental and neurodegenerative processes at work. Under such a parsimonious scheme, it is proposed that the underlying neurodevelopmental brain vulnerability predisposes to a more progressive brain loss.[23] A precedent for this viewpoint is Down syndrome (DS), which is a prototypical neurodevelopmental disorder caused by chromosomal abnormalities. Patients with DS show a variety of neurodevelopmental features clinically (see Table 5), and they also have mental retardation. Patients with DS develop Alzheimer's-like dementia very early on, typically in their 40s. Therefore, some have suggested that a 2-process model may also explain schizophrenia. But as elegant as each of these hypotheses are, they are also very difficult to prove or refute.

The weight of evidence currently favors a neurodevelopmental basis for schizophrenia. It is plausible that some patients could have a neurodevelopmental form of schizophrenia, while others may have a neurodegenerative schizophrenia.[20] The complexity of the process involved and the lack of a clear understanding lessen our ability to give a clear picture about schizophrenia to the public.

Brain Chemistry and Schizophrenia

Overactivity of the dopamine neurotransmitter system is the most compelling neurochemical abnormality in schizophrenia.[24] This is also the most easily explained

Table 7 Selected First- and Second-Generation Antipsychotic Medications: General Information*

Drug class	Drug name	Generic available?	Initial dose†	Maintenance dose†	Maximum dose‡	Cost of 30-day supply of oral drugs§
First-generation (typical) agents						
	Haldol (haloperidol)	Yes	1-5 mg	5-25 mg/d	60 mg/d	$
	Haldol long-acting injection	No	25-50 mg IM	50-200 mg IM, for 2-4 wks	300 mg IM, for 3-4 wks	
	Trilafon (perphenazine)	No	4-8 mg	16-56 mg/d	64 mg/d	$$
	Melleril (thioridazine)	Yes	50-100 mg	300-800 mg/d	800 mg/d	$$
	Stelazine (trifluoperazine)	Yes	2-5 mg	2-20 mg/d	20 mg/d	$$
	Loxitane (loxapine)	Yes	20 mg	50-100 mg/d	150 mg/d	$$$
	Moban (molindone hydrochloride)	No	20 mg	50-100 mg/d	150 mg/d	$$$$
Second-generation (atypical) agents						
	Clozaril (clozapine)	Yes	12.5-25 mg	150-600 mg/d in 2-3 divided doses	900 in 2-3 divided doses	$$$$
	Abilify (aripiprazole)	No	10-15 mg	10-30 mg/d	30 mg/d	$$$$$
	Abilify injection acute acting	No	5.25-9.75 mg IM	5.25-15 mg IM	30 mg IM, ≤10 hrs	
	Geodon (ziprasidone)	No	40-80 mg	40-160 mg/d	160 mg/d	$$$$$
	Geodon injection acute acting	No	10-20 mg/d IM	10-20 mg/d IM	40 mg/d IM (not studied for >3 days)	
	Invega XR extended release (paliperidone)	No	3-6 mg	3-12 mg/d; titrate up in 3-mg increments	12 mg/d	$$$$$
	Risperdal (risperidone)	No	1-2 mg	3-6 mg	16 mg/d	$$$$$
	Risperdal long-acting injection	No	25 mg IM (w/ oral Risperdal)	25 mg IM every 2 wks	50 mg IM every 2 wks	
	Seroquel (quetiapine)	No	50-100 mg	300-600 mg/d in 2-3 divided doses	800 mg/d in 2-3 divided doses	$$$$$
	Seroquel XR extended release	No	50-100 mg	300-800 mg/d	800 mg/d	$$$$$
	Zyprexa (olanzapine)	No	5-15 mg	10-40 mg/d	40 mg/d	$$$$$
	Zyprexa injection acute acting	No	2.5-10 mg IM	5-10 mg/d IM	30 mg/d IM in 3 mg 2-3 hrs apart	

IM indicates intramuscular.

*This is not an exhaustive list of the first-generation antipsychotics and is not intended to be used as a guide for dosing decisions.
†The dosing profiles for initial and maintenance treatments represent reasonable clinical practice; however, clinicians should consult the current *Physicians' Desk Reference* (*PDR*) and related regulatory sources for specific recommendations.
‡These doses represent current clinical practice, meaning that in some cases the dose is above the US Food and Drug Administration (FDA)-recommended upper-limit dose for that agent. Please also consult the FDA, other regulatory sources, and *PDR*. Dosing profiles tend to change over time as more information and research results become available.
§Cost estimates vary considerably. Please consult formulary information and/or the local pharmacy.

Cost key:
$ 0-25
$$ 26-50
$$$ 51-100
$$$$ 101-200
$$$$$ >200
Source for cost: Lexi-Comp, at www.drugstore.com.

Table 8 Safety and Tolerability of First- and Second-Generation Antipsychotics

Effect	Typical agents	Aripiprazole (Abilify)	Clozapine (Clozaril)	Olanzapine (Zyprexa)	Quetiapine (Seroquel)	Risperidone (Risperdal)	Ziprasidone (Geodon)
Extrapyramidal syndrome	+-+++	++	±	±-+[1]	±	±-+++[1]	±-+[1]
Tardive dykinesia	+++	± (?)	±	± (?)	± (?)	±-+	± (?)
Somnolence	±-+++	++	+++	++	+++	±	±
Prolactin	+++	–	±	+	±	+++	±
Weight gain	±	±	++++	+++	++	+	±
Dyslipidemia	±	±	++++	+++	++	+	±
Diabetes	±	±	++++	+++	++	+	±
QTc interval prolongation	±	±	++	+	+	+	++
Orthostatic blood pressure	±	+	+++	+	±	++	±

1. Indicates dose-related; –, none; ±, none/minimal; +, mild; ++, moderate; +++/++++, marked compared with placebo.
Note: This table gives an overall impression of the side-effect profile. For individual drugs, clinicians should consult the approved product labeling and/or the most current *Physicians' Desk Reference* manual.

theory for the public—people become psychotic because their dopamine is overactive. There is certainly evidence for this, including functional brain-imaging studies that show excess of dopamine in the brain of patients when they are acutely psychotic. But like all the other explanations of schizophrenia, it is not quite as simple as "too much dopamine." Some researchers have suggested there is overactivity of dopamine in one brain region (eg, temporal lobes), concomitant with underactivity in another area (eg, frontal lobes). Also, the fault may not be across all dopamine receptors but perhaps selectively in some of the subclasses of dopamine receptors or beyond the actual receptors, even as a subsequent maleffect in cell-signaling.

It is clear that other neurotransmitter systems are affected in schizophrenia. The neurotransmitter systems implicated in this disease are:

- Cholinergic
- Dopamine
- Glutamatergic
- Noradrenergic
- Serotonin.

Deficits in other neurotransmitter systems (eg, glutamate receptors) may underlie schizophrenia directly and/or indirectly through their interrelated effects on the dopamine system.[25] Thus far, the dopamine system has been the most pronounced neurochemical abnormality and, significantly, appears to be related to how patients respond to treatment.

Treatment of Schizophrenia

It is hardly surprising, given the complexity of the condition, that effective treatment of schizophrenia requires attention to multiple components of care. It is true that medications form the bedrock of treatment, but medications alone are not enough to keep people stable and/or to achieve recovery.[1,3,26,27] Elements of comprehensive care for patients with schizophrenia are listed in **Table 6**.

Antipsychotic medications

Antipsychotic medications are the mainstay of treatment (**Table 7**). Although all currently available antipsychotics act on the dopamine system (invariably to block dopamine D_2 receptors and are therefore considered to work by "turning off" the overactive dopamine receptors), this is likely to be too simplistic. Antipsychotic medications also have a variety of agonist (activating) and antagonist (deactivating) effects on several other neurotransmitters. Pharmaceutical companies have targeted the development of highly selective drugs (eg, a dopamine D_4 antagonist) or more "gunshot" drugs that have effects at multiple receptors ("pleomorphic" antipsychotics, such as clozapine [Clozaril] or olanzapine [Zyprexa]). The exact "magic potion" for treating schizophrenia remains a mystery. For now, the available medications are effective, but with limitations (**Table 8**).

A thorough account of the psychopharmacology of schizophrenia is beyond the scope of this article. Some

general comments on the treatment of schizophrenia are more appropriate.

1. With the exception of clozapine, the other antipsychotics are more similar than different in their ability to control the symptoms of schizophrenia.[28,29] All of them are effective in relieving acute symptoms—anxiety, agitation, delusions, and hallucinations. Some may act a bit quicker (or perhaps are easier to get quicker to an effective dose) and some may be more powerful in their effect on symptoms (again, dosing may play a big role here).

The older (also known as conventional, typical, or first-generation) antipsychotic medications have proved efficacy and work best against positive symptoms, with little benefit for negative, depressive, or cognitive symptoms (they may even worsen these aspects of the illness). Their major adverse side effects are related to their antagonism of the dopamine system. These drugs cause acute and chronic muscle (extrapyramidal) side effects that are distressing and disfiguring. Because they have been around for a long time, they are relatively inexpensive.

The new antipsychotics, also known as atypical or second-generation antipsychotics, show similar or slightly better efficacy compared with the first-generation agents in treating positive symptoms. They have variable, but generally only modest, benefits in treating negative, depressive, and cognitive symptoms. Although these medications generally have a lower risk for extrapyramidal side effects than the first-generation agents, they have other serious side effects, as reflected in Table 8.

More so than the first-generation antipsychotics, the newer agents cause weight gain and metabolic disturbances of glucose, insulin, cholesterol, and lipids.[29,30] This is a major drawback, which has substantially complicated the treatment of schizophrenia and is currently the number-one issue in the psychopharmacology of schizophrenia. Treating physicians are monitoring patients carefully to detect such disturbances and are also concerned about switching medications and seeking relief in another antipsychotic when these problems emerge.

These drugs are also remarkably expensive, which limits access and imposes high financial burden on an already overburdened mental healthcare system. In contrast, if these (or any particular) drugs keep a patient from relapsing and avoiding hospitalization, then the medication is cost-effective.

2. Although antipsychotics are generally effective (better in acute care and for positive symptoms), a substantial group of patients remains unwell. Some patients relapse frequently over time; some are chronically psychotic, and the medications barely work for them. Efforts to help these patients include:

- Trials of high doses of an antipsychotic
- A trial of 2 antipsychotics together
- Trials of add-on drugs (eg, antidepressants, stimulants) that may boost the effect of the antipsychotics
- Use of clozapine (the most powerful of all antipsychotics but with a high side-effect burden)
- For intractable situations, as well as for severe depression or catatonia, a trial of electroconvulsive therapy.

There is also a particular interest at present in finding ways to reduce the cognitive deficits of schizophrenia, which are rate-limiting obstacles to recovery.[31]

3. The side-effects burden of the antipsychotics is substantial. Clinicians engage in a trial-and-error process with patients in an effort to find the drug that will work best and will result in fewer side effects. The sensitivity of each patient is unique—both in terms of the ability to respond to one drug (but perhaps not to another) as well as to experience the side effects.

The response and tolerability of each patient is individualized. We can make general predictions about the overall risk-benefit profile of any given drug, but how a patient will fare in practice is the true test. In addition, the dose of the medication strongly influences both response and tolerability. At present, the selection, dosing, and use of antipsychotics in clinical practice are more art than science. Efforts toward personalized medicine and toward the emergent strategy of pharmacogenetics (the genetics of medication response and side-effect prediction) offer future hope.

4. Regardless of the benefits and drawbacks of the medications themselves, our ability to treat schizophrenia is curtailed even more by the patient's reluctance to take antipsychotic drugs and to continue using medications.[32] Estimates differ by each study, but approximately 50% of patients are noncompliant with their prescribed antipsychotic medication regimen.[33] Most are partially noncompliant, missing medications "here and there." Some patients are noncompliant and "learn the hard way," by having recurrent relapses of illness. Some patients remain noncompliant with treatment and, as a result, are extremely difficult to treat.

When at imminent risk to themselves or others, patients can be hospitalized against their will and be forcibly medicated until their illness is stabilized. The problem then recurs, however, when they are discharged from the hospital. To combat medication noncompliance, patients can receive their antipsychotic medication in an injectable form that provides contin-

Table 9 Psychiatric and Medical Conditions Associated with Schizophrenia

Anxiety and (less commonly) obsessions/compulsion
Cardiovascular disorders
Depression
Metabolic disturbances
Obesity
Sexual behavior associated with HIV, hepatitis C infection
Smoking
Substance abuse
Suicidality
Violence

uous treatment over weeks, usually 2 to 4 weeks. Some clinicians believe that this strategy is underutilized and should become more mainstream rather than be confined to patients who refuse their medications.

Comorbidities complicate treatment

In addition to the complexity of the illness itself, patients with schizophrenia are likely to have other psychiatric and/or medical comorbidities over the course of their illness, as outlined in **Table 9**.

Social aspects of treating mental illness

Beyond medications, patients need a huge amount of support.[34] The greatest support patients can get—and do get—is from their families. Relatives provide love, emotional support, housing, and financial assistance. They are also the people who know the patient best and can be watchful for signs of relapse. However, the emotional strain of caring and living with someone who is suffering from schizophrenia can be overwhelming. Relatives also need support. They need education on the latest treatments, as well as tips on how to manage difficult situations. Organizations such as the National Alliance for Mental Illness are an invaluable resource.

Patients also need psychological support from mental health professionals. Patients benefit from counseling and supportive psychotherapy. There are also programs that focus on social skills training, helping patients to make friends and to reintegrate into the community. Most patients do not work; if they do, it is often at a low-paying job. Although it is clear that active psychosis and cognitive deficits reduce the capacity of people to hold down jobs (especially stressful jobs), it is also evident that having a job is a powerful motivator for healthy living and boosts self-esteem.

There are now efforts to train people and to enhance their cognitive abilities so that they will be able to sustain in employment.[35] Our system is poorly constructed to help people get, and hold jobs. Sometimes patients are faced with the painful decision of taking a job and losing their Medicaid support, because they now earn a wage. These situations expose some of the many ways that our society discriminates against people with mental illness.

Similar to the role of sponsors in Alcoholics Anonymous, patients with serious mental illness are now also helping other patients to recover.[36] These "peer-support specialists" can be powerful catalysts for change, for individual patients and for systems of care through their roles as advocates. This is a powerful approach that broadens the focus of care toward more meaningful, life-attainment goals. It also instills personal responsibility and hope in patients.

Hope is a powerful catalyst in coping with illness. The notion that some people can recover from serious illnesses like schizophrenia is powerful.[37] Important components of recovery for people with serious mental illness include hope, spirituality, and empowerment.[37]

Patients with more severe illness require continuous support to help them live in the community. This service is delivered by a community psychiatric team comprised of case managers, with each team serving just a few patients. This labor-intensive approach, called "assertive community treatment" (ACT), works well to maintain patients in the community. Although its staffing costs are high, it is still cost-effective, because ACT dramatically reduces days spent in a hospital.

Conclusion

Schizophrenia is a challenging condition to diagnose and to treat. The lack of insight that is so common with the condition could undermine (through treatment nonadherence) the efforts of family and mental health professionals to provide comprehensive care. The potential for comorbidities further adds to the complexity of the illness and will require additional psychiatric and/or medical treatment. These further complicate already arduous clinical circumstances. Patients with schizophrenia need comprehensive care, compassion, and support. They deserve this. ■

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AHDB Stakeholder Perspective

The Approach to Schizophrenia

PAYORS: Payors have had a difficult time understanding how to approach schizophrenia. In the private sector, payors are accustomed to taking action when possible. Employers expect contracted insurance companies to take action on their behalf whenever it makes sense. This disease state, however, does not lend itself to such a direct treatment approach. Patients with schizophrenia-related disorders are often reluctant to adhere to medication regimens. The results are often viewed in one of two ways: The sick member who avoids medication, or the sick member who takes expensive medications in a nonadherent manner—both of which result in less-than-optimal health.

The major payors in this arena are state Medicaid agencies. Medicaid dollars pay for a substantial amount, perhaps half, of all prescriptions for schizophrenia, and must then pay for all related healthcare

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costs. So what are the goals of these state agencies? The states seek to ensure that people have access to care. Unfortunately, effectiveness is secondary to access.

This theme seems to be consistent regardless of who the payor is—private or public. As we do for other disease states, the payor community should push for a metric that demonstrates effective care for the patient with schizophrenia. Granting access to a random assortment of nonadherent monotherapies and combination therapies is not the answer. We should strive to ensure that patients and their providers make valiant attempts at treatment protocols before abandoning them in favor of the next horse on the schizophrenia drug carousel.

In the 1970s, advocates fought against the use of "depo-products" (eg, injected haloperidol) on the basis that some patients were overmedicated, and that one did not have the ability to immediately reverse the course of treatment if desired when using such extended-release products. Over the past 35 years, reverting to daily oral medications as standard treatment has witnessed the reemergence of patient nonadherence. A call for a return to forced medication has now been heard to redress the situation. Where shall it go from here?

PATIENTS: Ultimately, the direction should be determined by what is best for the patient. Neither legal advocates interested in outlawing extended-release medications as a civil rights infringement, nor state agencies willing to throw the entire medicine cabinet at patients without regard to medication effectiveness, should be making this decision.

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Prior Authorization for Antipsychotics Complicates Adherence

BENEFIT MANAGERS: The question of open versus restrictive access to the newer (atypical) antipsychotic medications lingers, as prior authorization (PA) and step-edit policies are being used to control costs,[1] and nonadherence remains a major concern. In his article, Dr Buckley notes that schizophrenia is the most serious mental condition, which requires optimal therapy.

Findings from a study just published in *Health Affairs* and led by Dr Steven B. Soumerai of Harvard Medical School's Department of Ambulatory Care and Prevention "provide strong evidence of both intended and unintended consequences of the Maine PA policy"[2] implemented in a Medicaid program from July 2003 through March 2004. Dr Soumerai and colleagues compared antipsychotics use in the Maine program pre- and postimplementation of the PA policy; an open access Medicaid program in New Hampshire was used as control. The Maine PA policy resulted in a 29% greater risk of treatment discontinuation compared with the period before implementing the PA policy.[2] No differences in discontinuation risk were found in the New Hampshire program.

The authors concluded that "the most adverse clinical outcome was treatment discontinuation, which is a strong predictor of acute psychotic episode, hospitalization, and other negative clinical and economic outcomes. Pharmacy savings were minimal."[2] They admit that restrictive policies may control costs when applied to more homogeneous drug classes (eg, nonsteroidal anti-inflammatory drugs or angiotensin-converting enzyme inhibitors), but because of marked differences in patients' response to antipsychotics, such tools are not productive and can be harmful when used for antipsychotics the authors say. In an interview with Newswire, Dr Soumerai said, "Given the tremendous variation in individual responses to these drugs as well as the devastating impact of treatment disruption on schizophrenic patients, a policy that pushes all patients toward a limited number of preferred drugs may do more harm than good."[3]

More than 30% of Medicare Part D and Medicaid programs have PA policies for antipsychotics.[1,2]

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